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TWELFTH EDITION

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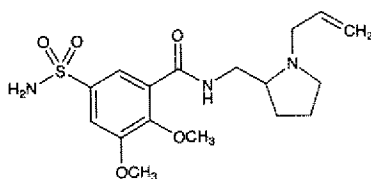
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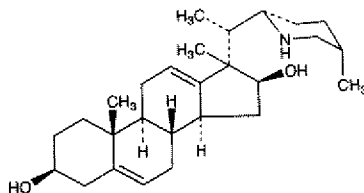
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naud, J. Macler, *ibid.* 57, 353 (1981); S. Angeli, P. Fougère, *ibid.* 58, 111 (1982).



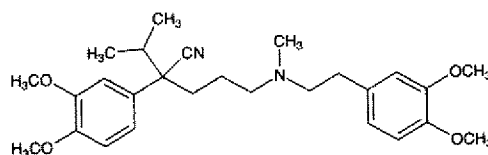
THERAP CAT: Treatment of menopausal disorders.

10082. Veralkamine. (3 β ,16 β ,17 α ,22 α)-17-Methyl-18-nor-16,28-secosolanida-5,12-diene-3,16-diol; 17-methyl-20 α -(2S,5S)-5-methyl-2-piperidyl-18-nor-17 α -pregna-5,12-diene-3 β ,16 β -diol; (22S:25S)-12,26-epimino-17 β -methyl-18-nor-cholesta-5,12-diene-3 β ,16 β -diol; (17S:12S:25S)-22,26-epimino-18(13-17)-abeo-cholesta-5,12-diene-3 β ,16 β -diol; veralkamine. $C_{27}H_{43}NO_3$; mol wt 413.64. C 78.40%, H 10.48%, N 3.39%, O 7.74%. Steroidal alkaloid isolated from *Veratrum album* sp. *lobelianium* (Bernh.) Suessenguth, *Liliaceae*: Tomko et al., *Pharm. Zentralhalle* 99, 373 (1960), *C.A.* 55, 2013c. Structure studies: Tomko et al., *Coll. Czech. Chem. Commun.* 27, 1404 (1962). Complete structure: Tomko et al., *Tetrahedron Letters* 1967, 3907; *ibid.* *Tetrahedron* 24, 4865 (1968); Hoehne et al., *ibid.* 4875.



Crystals from ethanol, mp 119-123° and 165-169°; $[\alpha]_D^{25}$ -84.1° \pm 3 (c = 0.533 in $CHCl_3$). *N,O,O*-Triacetate, mp 152-154°. $[\alpha]_D^{25}$ -8.0° ($CHCl_3$). *N*-Monoacetate, mp 191-193°. $[\alpha]_D^{25}$ -79.1° ($CHCl_3$).

10083. Verapamil. α -[3-[[2-(3,4-Dimethoxyphenyl)ethyl]methylamino]propyl]-3,4-dimethoxy- α -(1-methylethyl)-benzenecarbonitrile; 5-[(3,4-dimethoxyphenethyl)methylamino]-2-(3,4-dimethoxyphenyl)-2-isopropylvaleronitrile; α -isopropyl- α -[(*N*-methyl-*N*-homoveratryl)- γ -aminopropyl]-3,4-dimethoxyphenylacetonitrile; iproveratril; D-365. $C_{27}H_{35}N_2O_4$; mol wt 454.61. C 71.34%, H 8.43%, N 6.16%, O 14.08%. Coronary vasodilator with calcium blocking activity. Prepn: Belg. pat. 615,861; Dengel, U.S. pat. 3,261,859 (1962, 1966 both to Knoll). Physical and chemical data: Appel, *Arzneimittel-Forsch.* 12, 562 (1962). Synthesis and absolute configuration of enantiomers: Ramuz, *Helv. Chim. Acta* 58, 2050 (1975). Stereospecific synthesis of enantiomers: L. J. Theodore, W. L. Nelson, *J. Org. Chem.* 52, 1309 (1987). Pharmacology: Haas, Hartfelder, *ibid.* 549; Schieper, Witzleb, *ibid.* 559. Metabolism: McIlhenny, *J. Med. Chem.* 14, 1178 (1971). HPLC determin in plasma: C. Horne et al., *Arzneimittel-Forsch.* 37, 956 (1987). Series of articles on clinical studies: *ibid.* 20, 1277-1336 (1970). Comparative study in variant angina: D. D. Waters et al., *Am. J. Cardiol.* 47, 179 (1981); in arrhythmias: B. N. Singh et al., *Drugs* 25, 125 (1983). Symposium on pharmacology and clinical efficacy in hypertension: *Am. J. Cardiol.* 57, 1D-107D (1986). Comprehensive description: Z. L. Chang, *Anal. Profiles Drug Subs.* 17, 643-674 (1988). Reviews: S. H. Baky, E. B. Kirsten, in *Pharmacological and Biochemical Properties of Drug Substances* vol. 3, M. E. Goldberg, Ed. (Am. Pharm. Assoc., Washington, DC, 1981) pp 226-261; D. J. Triggle, V. C. Swamy, *Circ. Res.* 52(2), Pt. 2, 117-128 (1983).

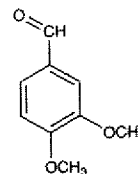


Viscous, pale yellow oil, bp_{0.61} 243-246°. n_D^{25} 1.5448. Practically insol in water. Sparingly sol in hexane; sol in benzene, ether. Freely sol in the lower alcohols, acetone, ethyl acetate, chloroform.

Hydrochloride, $C_{10}H_{10}N_2O_4 \cdot HCl$, *Arpamyl*, *Berkatens*, *Calan*, *Cardiagut*, *Cardibeltin*, *Cordilox*, *Dignover*, *Dros-teakard*, *Geangin*, *Isopstin*, *Quasar*, *Securon*, *Univer*, *Vasolan*, *Veracim*, *Veramex*, *Verapin*, *Verelan*, *Verexamil*. Crystals, dec 138.5-140.5° (corr). Soly (21°): 7 g/100 g water (pH = 4.24). pH of 0.1% aq soln: 5.25. uv max: 232, 278 nm. Sparingly sol in chloroform. Sol in ethanol, isopropanol, acetone, ethyl acetate; freely sol in methanol, DMF. Soly (mg/ml): water 83, ethanol (200 proof) 26, propylene glycol 93, ethanol (190 proof) >100, methanol >100, 2-propanol 4.6, ethyl acetate 1.0, DMF >100, methylene chloride >100, hexane 0.001. pKa 8.6. LD₅₀ in rats, mice (mg/kg): 16, 8 i.v. (Baky, Kirsten).

THERAP CAT: Antianginal; antiarrhythmic (class IV).

10084. Veratraldehyde. 3,4-Dimethoxybenzaldehyde; 3,4-dimethoxybenzenecarbonal; veratric aldehyde; protocatechualdehyde dimethyl ether. $C_9H_{10}O_3$; mol wt 166.18. C 65.05%, H 6.07%, O 28.88%. Prepd by methylation of vanillin: Kostanecki, Tambor, *Ber.* 39, 4022 (1906); Buck, *Org. Syn.* 13, 102 (1933); Alt. U.S. pat. 3,007,968 (1957 to Monsanto); by oxidation of veratryl alcohol with chromium(VI) oxide-pyridine complex: Holum, *J. Org. Chem.* 26, 4814 (1961).



Needles from ether, petr ether, toluene, or carbon tetrachloride. Odor of vanilla beans; mp 42-43°; bp₇₆₀ 281°; bp₅₀ 201°; bp₁₀ 155°. Slightly sol in hot water; freely sol in alcohol and ether. Solns are oxidized to veratric acid under the influence of light.

10085. Veratramine. (3 β ,23 β)-14,15,16,17-Tetradehydro-veratraman-3,23-diol. $C_{27}H_{39}NO_3$; mol wt 409.61. C 79.17%, H 9.60%, N 3.42%, O 7.81%. Secondary base from *Veratrum grandiflorum* (Maxim.) Loes. f., and from *V. viride* Ait., *Liliaceae*. Isoln and structure: Saito, *Bull. Chem. Soc. Japan* 15, 22 (1940); Jacobs, Craig, *J. Biol. Chem.* 160, 555 (1945); Jacobs, Sato, *ibid.* 181, 55 (1949); 191, 71 (1951); Tamm, Wintersteiner, *J. Am. Chem. Soc.* 74, 3842 (1952); Wintersteiner, *Festschrift Arthur Stoll* (Birkhäuser-Verlag, Basel) pp 166-176. Total synthesis: Masamune et al., *J. Am. Chem. Soc.* 89, 4521 (1967); Johnson et al., *ibid.* 4523; Masamune et al., *Tetrahedron* 27, 3369 (1971); Kutney et al., *Can. J. Chem.* 53, 1796 (1975). Stereochemistry: Sicher, Tichy, *Tetrahedron Letters* 1959(12), 6 (1959); Kataoka, Chem. & Ind. (London) 1961, 512; Bailey et al., *Tetrahedron Letters* 1963, 555. Revised stereochemistry: Scott et al., *ibid.* 1967, 2381; Kupchan, Suffness, *J. Am. Chem. Soc.* 90, 2730 (1968); Sprague et al., *Tetrahedron* 27, 4857 (1971). See also: *Veratrum Viride*.